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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,669	12/21/2001	Rama Akella	SBI-111	1708

7590 03/26/2003

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,669	AKELLA ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The drawings are objected to because in the caption to Figure 2, "povidone" is misspelled. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

2. The disclosure is objected to because of the following informalities: At page 1, line 2, the filing date should be inserted after "09/748,038". The abbreviation "GFM", used in the caption to Figure 3, does not appear to be defined in the specification. Appropriate correction is required.

3. Claims 13 and 20-22 are objected to because of the following informalities: At claim 13, line 2, a comma should be inserted between "BMP-7" and "TGF-". In claims 20, 21, and 22, line 1 of each claim, "comprising" should be changed to "comprises". Appropriate correction is required.

4. The effective filing date of instant claims 1-31 is deemed to be December 21, 2001, the filing date of the instant application. Instant claims 1-31 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/748,038 because the parent application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the genus of TGF-β superfamily polypeptides; does not disclose vinyl pyrrolidone polymers in general; does not disclose the molecular weight range of about 2.5 kD to about 20 kD; does not disclose water or aqueous buffer solutions as solvents for the growth factor composition; does not disclose the polymer concentration range of about 0.1% w/v to about 70% w/v or the narrower ranges of instant claims 8-10; does not disclose the viscosity ranges recited in instant claims 26-29; does not disclose promoting soft tissue regeneration in general; and does not disclose increasing the

bioavailability of growth factors. Accordingly, U.S. Patent Application Publication 2002/0040004, which was published based upon parent application 09/748,038 and has a different inventorship than the instant application, is available as prior art against the instant claims under 35 U.S.C. 102(e).

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In

addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

6. Claims 1-19 and 23-31 are rejected under 35 U.S.C. 103(a) as being obvious over the Mueller et al article (Swiss Med. Wkly., Vol. 131, pages 23-25). The Mueller et al article teaches a bone protein mixture, which includes angiogenic factors such as FGF and TGF-β, in combination with a 5% solution of povidone. The composition is injected into the myocardial tissue of pigs and results in angiogenesis. See, e.g., the Abstract and page 24, column 1, first paragraph. Because the Mueller et al article does not specify a solvent for the 5% povidone solution used therein, the solvent inherently will be either water or an aqueous buffer solution. The Mueller et al article's source of bone proteins, Provasc from Sulzer Carbomedics, is the same as Applicants' disclosed source of growth factor (see page 17, line 16), and the Mueller et al article discloses its Provasc to comprise a mixture of angiogenic factors. In view of the similarity in source and composition between the Mueller et al article's source of bone proteins and Applicants' disclosed and claimed growth factor mixtures, the two are deemed to be the same and the Mueller et al article's source of bone proteins is deemed inherently to comprise the same mixture of growth factors claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the Mueller et al article's source of bone proteins and Applicants' claimed mixture of growth factors to shift the burden to Applicants to provide evidence that their claimed mixture of growth factors is unobviously different than the Mueller et al article's source of bone proteins. The Mueller et al article does not teach a molecular weight for the povidone, does not teach povidone concentrations range from about 0.5% w/v to about 2.5% w/v, does not teach administering the composition to human patients in need of angiogenesis, and does not

teach a viscosity for the povidone solutions. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal molecular weights and concentrations for the povidone solutions of the Mueller et al article, because molecular weight and concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer and pharmaceutical arts. Such a determination would at the same time result in an optimization of the viscosity of the polymer-containing solution. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the compositions of the Mueller et al article to induce angiogenesis in ischemic myocardial tissue in human patients because it is desirable to induce angiogenesis in such patients so as to restore blood flow to the injured organ, and because the pig subjects of the Mueller et al article are in vivo models which are reasonably predictive of success in human patients. With respect to instant claim 30, myocardial and heart tissue are soft tissues. With respect to instant claim 31, the Mueller et al article adds bone protein to the solvent containing povidone rather than adds povidone to the solvent containing povidone. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to add the bone protein and povidone of Mueller et al to the solvent in any order because the order of adding solutes to the solvent would not have been expected to have any effect on the properties of the resulting solution, and because changes in the sequence of adding ingredients are prima facie obvious. See MPEP 2144.04(IV)(C).

7. Claims 13-15 and 20-22 are rejected under 35 U.S.C. 103(a) as being obvious over the Mueller et al article (Swiss Med. Wkly., Vol. 131, pages 23-25) as applied against claims 1-19 and 23-31 above, and further in view of the U.S. Patent Application Publication 2002/0040004.

To the extent that the Mueller et al article does not teach the use of the growth factor mixtures of instant claims 13 and 15, the U.S. Patent Application Publication '004 teaches a preference for using a combination of growth factors, especially a combination of BMP-2, BMP-3, BMP-7, TGF-β, and FGF, and optionally further comprising IGF-1, EGF, HGF, TGF-α, and PDGF, and teaches that the growth factors can be applied subcutaneously, intramuscularly, or intravenously. The growth factor mixture can also be administered in combination with a povidone carrier. See, e.g., paragraphs 0014-0016, 0044, 0075, 0077, and 0088, and claims 2, 6, and 8. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the combination of growth factors preferred by the U.S. Patent Application Publication '004 in the method of the Mueller et al article because the Mueller et al article discloses a preference for a mixture of growth factors because of possible synergy, and the U.S. Patent Application Publication '004 discloses a combination of growth factors which can be used for the same purpose and with the same carrier taught by the Mueller et al article. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the growth factor mixtures of the Mueller et al article by subcutaneous, intramuscular, or intravenous methods because these methods of administration are known methods which are less invasive than the injection method taught in the Mueller et al article, and because the U.S. Patent Application Publication '004 teaches that these methods of administration are also capable of promoting natural bypass in mammals.

8. Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by the Chemical Abstract 132:40522x. The Chemical Abstract 132:40522x teaches forming an aqueous solution of bone morphogenetic protein and combining it with a second aqueous solution of bFGF and

PVP. The resultant composition is used for osteogenesis stimulation. Because the same growth factor, solvent, and vinyl pyrrolidone polymer are combined according to the same method steps in the Chemical Abstract as in Applicants' claimed invention, inherently the bioavailability of the BMP in the Chemical Abstract will be increased to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the method of the Chemical Abstract and Applicants' claimed method to shift the burden to Applicants to show that the claimed method is unobviously different than that of the Chemical Abstract.

9. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being obvious over the Chemical Abstract 132:40522x. Application of the Chemical Abstract 132:40522x is the same as in the above rejection of claim 31. The Chemical Abstract 132:40522x does not teach a molecular weight or solution concentration for its PVP. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine a molecular weight and solution concentration for the PVP of the Chemical Abstract because molecular weight and solution concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer, solution chemistry, and pharmaceutical arts.

10. Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being obvious over the Chemical Abstract 132:40522x as applied against claims 1-12 above, and further in view of Poser et al (U.S. Patent No. 5,290,763) and Applicants' admission of the prior art at page 6, lines 22-25, of the specification. The Chemical Abstract 132:40522x does not disclose using the growth factor mixture specified in instant claims 13 and 15 in order to stimulate osteogenesis. Poser et al teach osteoinductively active mixtures of proteins used to induce or promote bone growth (see, e.g., column 1, lines 7-9; column 4, lines 15-17 and 33-38; and column 9, lines 54-

58). Applicants admit at page 6, lines 22-25, of their specification that Poser et al is a source of their preferred mixtures of bone proteins. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the osteoinductively active mixtures of proteins taught by Poser et al in place of the bone morphogenetic protein taught by the Chemical Abstract 132:40522x because the substitution of one known functional equivalent for another is prima facie obvious, and because the high osteoinductive activity disclosed by Poser et al for their protein mixtures (see Example 5) would have led one of ordinary skill in the art to expect a high degree of osteogenesis stimulation when used in the method of the Chemical Abstract 132:40522x.

11. The Prochazka et al abstract (J. Reproduction fertility, No. 25, page 64), the European Patent Application 516,901, Hanyu et al (U.S. Patent Application Publication 202/0009789), and the Wu et al article are cited as art of interest, but are deemed to be at best duplicative of the references applied above.

The Sakagachi et al article and the Wiley et al article are cited as art of interest; however, the molecular weight of their PVP (see page 1329, second full paragraph, of the Sakagachi et al article and page 385, third full paragraph, of the Wiley et al article) is significantly higher than permitted in instant claim 1. With respect to instant claim 31, the two articles are at best duplicative of the references applied above.

U.S. Patent No. 6,211,157, which issued based upon grandparent application 09/173,989, is not deemed to raise any issues of obviousness-type double patenting with the instant claims.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

March 24, 2003